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Purpose: To evaluate the significance of fractionated administration of thalidomide combined with γ-ray irradiation in terms of local tumor response and lung metastatic potential, referring to the response of intratumor quiescent (Q) cells.
Materials/methods: B16-BL6 melanoma tumor-bearing C57BL/6 mice were continuously given 5-bromo-2'-deoxyuridine (BrdU) to label all proliferating (P) cells. The tumor-bearing mice then received γ-ray irradiation after thalidomide treatment through a single or 2 consecutive daily intraperitoneal administrations up to a total dose of 400 mg/kg in combination with an acute hypoxia-releasing agent (nicotinamide, 1,000 mg/kg, intraperitoneally administered) or mild temperature hyperthermia (MTH, 40 centigrade for 60 minutes). Immediately after the irradiation, cells from some tumors were isolated and incubated with a cytokinesis blocker. The responses of the Q and total (= P + Q) cell populations were assessed based on the frequency of micronuclei using immunofluorescence staining for BrdU. In other tumor-bearing mice, 17 days after irradiation, macroscopic lung metastases were enumerated.
Results: Thalidomide raised the sensitivity of the total cell population more remarkably than Q cells in both single and daily administrations. Daily administration of thalidomide elevated the sensitivity of both the total and Q cell populations, but especially the total cell population, compared with single administration. Daily administration, especially combined with MTH, decreased the number of lung metastases.
Conclusions: Daily fractionated administration of thalidomide in combination with γ-ray irradiation was thought to be more promising than single administration because of its potential to enhance local tumor response and repress lung metastatic potential.

Keywords: Quiescent cell: Lung metastasis: Thalidomide

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The Malthus Project - updated predictions of national radiotherapy demand to 2030

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Purpose: The Malthus model is an evidence based simulation of radiotherapy demand in England, which was designed to estimate radiotherapy utilisation at local and national level, in order to assist in planning of radiotherapy services. The model utilised cancer registration data from the national cancer registration service, together with predictions of population growth from the Office of National Statistics, and cancer incidence projections. We present the results of an updated model that utilises the latest population projection estimates, and cancer incidence data.
Materials and Methods: Base data on cancer registration was provided by the National Cancer Intelligence Network, broken down by disease site, local Clinical Commissioning Groups (CCGs), age and sex. Equivalent population data was sourced from the Office for National Statistics. These two datasets were combined with data from 2,000 evidence-based clinical decisions, covering 22 different cancer sites. Clinical practice was peer-reviewed by over 100 British oncologists and at a national forum. An updated cancer incidence projection model and population projection model were also used to enable annual demand predictions up to 2035.
Results: The Malthus model estimates that the access rate for radiotherapy in England in 2015 should be 40.5% with a fraction burden of approximately 47,500 fractions per million population. To highlight how different regions within a country can be, Table 1 displays two regions and the England average for comparison. The predicted demand for radiotherapy is also increasing for England. Over the next few year the predicted fractions per million will increase by 0.9% per year, this will increase to 1% per year in 2020 and is expected to hit 1.1% per year by 2026.

	# per Million				
Region	All Sites	Breast	Lung	Prostate	H&N
England	47500	12500	5900	13100	4200
Dorset	65900	17000	6300	22600	5300
Tower Hamlets	19400	4000	3400	4000	3000

Table 1. Fractions per Million for the 'Big 4' for England and two different regions.

Conclusions: The Malthus model with updated cancer incidence data suggests a radiotherapy utilisation rate of 40.5%, with a predicted annual increase of fractions per million of around 1% per year. Whilst the observed rates of radiotherapy utilisation still lag behind the model's predictions, the observed activity increases in England (from the Radiotherapy Data Set) over the last 3 years exceed the rate of rise in predicted demand. Customised simulations for individual regions, such as what Malthus can do, allows local cancer profiles to be taken into account for more accurate current and future demand predictions. The customisability also allows for simulations looking at the impact of new technology, such as MRI Linac and Proton therapy, and data from other countries can be incorporated as well.
Keywords: Health Service Research, Demand Prediction

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Progress with MRI-linac image-guided radiation dose imaging

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Purpose: MRI-linacs will enable 4D image-guided radiotherapy and require accurate MR visible and compatible dosimeter systems for verification.
Methods: Motion-tracking utilising a MagicPlate (M512) silicon array dosimeter capable of high resolution dosimetry (Petasecca, 2015) (figure 1a,b)has been modified for purpose of MR imaging during dynamic detector-tracking (i.e. so named 'MR guided dynamic dosimaging'). The detector was tested for MRI-safety and functionality without irradiation in a 1T fringe field of 3T Siemens Skyra MRI. As solid water can not be visualized on MRI a tissue-equivalent, gel-water phantom (CIRS® Computerized Imaging Reference Systems Inc. VA, USA), providing signal for detector and fiducial visualisation, was utilised to enable MR imaging (fast spin echo sequence).
Results: MR images of a non-powered detector system demonstrated detector visualization (see figure 1c). Detector movements approximating breathing were also acquired during dynamic MRI acquisition (fast gradient echo), showing that fiducial markers could be visualised when placed on a passive device and tracked. The detector functioned at the 1T bore entry position to simulate the magnetic field of our impending MR linac whilst a water phantom was imaged simultaneously at the mid-bore 3T position, with noise (see figure 1d) seen due to detector RF interference being reduced by aluminium foil shielding of the device and cables (figure 1e).
Conclusions: The current MRI-guided dynamic dosimaging set-up has been demonstrated to be successful in detector visualisation and tracking with a non-powered detector. Noise reduction has been achieved with the detector in operational mode. A MRI-compatible motion platform will be paired with M512. These measurements will be compared to acquisition in MRI-linac magnetic fields on the MRI-linac device being installed at the Ingham Institute in Australia.

Keywords: Radiotherapy, MRI-linac, dosimetry

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